

# Education and debate

## The marketing of a disease: female sexual dysfunction

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The pharmaceutical industry's dreams of making large profits from treating female sexual dysfunction are starting to look like premature speculation

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Robert Wilson's bestselling book *Feminine Forever* helped persuade the modern world that the menopause was a "disease" of hormone deficiency, to be cured with hormone replacement.<sup>1</sup> The book's 1966 front cover promised, "Every woman no matter what her age, can safely live a fully-sexed life for her entire life," and the hormones sold by Wilson's sponsor duly became best sellers. Forty years later, long term hormone replacement has been exposed as doing more harm than good, drug sales have collapsed, and Wilson's thesis is rightly ridiculed as corporate sponsored disease mongering.<sup>2,3</sup>

In the shadows of this overmedicalisation, the pharmaceutical industry is meeting unexpected resistance to its attempts to sell women the next big profitable "disease," female sexual dysfunction. This condition is claimed by enthusiastic proponents to affect 43% of American women,<sup>4</sup> yet widespread and growing scientific disagreement exists over both its definition and prevalence. In addition, the meaningful benefits of experimental drugs for women's sexual difficulties are questionable, and the financial conflicts of interest of experts who endorse the notion of a highly prevalent medical condition are extensive. These controversies have been brought into focus by the rejection of Proctor and Gamble's experimental testosterone patch by advisers to the US Food and Drug Administration in December 2004.<sup>5</sup>

### Controversy about the condition

The first step in promoting a blockbuster drug is to build the market by raising public awareness about the condition the drug is designed to target.<sup>6</sup> In anticipation of regulatory approval of its testosterone patch—the first drug assessed for female sexual dysfunction—Proctor and Gamble unleashed a multilayered global marketing campaign. It sponsored key scientific meetings in sexual medicine, hired leading sex researchers as consultants, funded continuing medical education activities, produced a reporter's guide to testosterone, and created a publicly accessible website. It has worked with agents from three public relations companies and at least one major advertising firm to promote awareness of both the "disease" and the drug.

Proctor and Gamble's patch spokesperson, Elaine Plummer, told me that this is "Not an exceptional amount of firepower." Some industry reports suggest,



however, that the company may have already set aside an initial \$100m (£53m, €76m) to spend on advertising alone.<sup>7</sup> Long before its testosterone patch had even been assessed for approval, the company's global marketing had been strategically targeting health professionals, reporters, and the general public, seeking to shape their perceptions of female sexual problems and how to treat them.

"The product the company is selling at this stage is really the disease," argues Leonore Tiefer, a psychologist and clinical associate professor at New York University School of Medicine. "I think Proctor and Gamble has a marketing plan that worked for shampoo. Create a buzz, get the word out, heighten consciousness, get people talking," she said. Since it has been hoping to have the first approved drug solution, says Tiefer, "it only has to get people talking about the condition, and present it as amenable to a drug intervention. Then it won't be seen as the company pushing its product, it will be seen as health education."

Proctor and Gamble has been seeking specific approval from the Food and Drug Administration (FDA) to market testosterone to women who have had their ovaries removed and are taking oestrogen. Such women may apparently suffer from a subdisorder of female sexual dysfunction called hypoactive sexual desire disorder. Many of the company's initial marketing efforts have been designed to educate doctors and the public about these conditions. Yet although both conditions are listed in the *Diagnostic and Statistical*

*Manual of Mental Disorders*, both are controversial. Some Australian sex researchers have described the whole concept of sexual dysfunction as questionable because it downplays relational and cultural factors,<sup>8</sup> and a group of the world's key figures in female sex research, led by Rosemary Basson, recently criticised hypoactive sexual desire disorder, describing it as a "problematic" diagnosis because it failed to fully encompass contemporary understandings of the complexity of women's sexual responses.<sup>9</sup>

Although agreeing that sexual difficulties may sometimes be due to a medical condition, John Bancroft, a former director of the Kinsey Institute, dismisses the notion of a dysfunction affecting 43% of women as outrageous. "It doesn't stand up scientifically," he said. He argues that reductions in sexual interest or other problems are often healthy adaptive responses and "an understandable reaction to adverse conditions in the relationship ... or in the individual's general life situation."<sup>10</sup> Because of the difficulty distinguishing between a genuine dysfunction and a healthy adaptive response, any survey based estimates of the condition's prevalence are, he says, unreliable.

The extent of this scientific disagreement and uncertainty is not reflected in the scientific and educational materials sponsored by Proctor and Gamble. Slides from the sponsored medical education package currently being delivered to doctors in the United States, called "Renewing sexual desire: understanding HSDD in postmenopausal women," do not mention the critical work of leading researchers including Tiefer and Bancroft. More importantly, the education package cites older work from Basson and colleagues without referencing their more recent revisions which describe hypoactive sexual desire disorder as a problematic diagnosis.<sup>8</sup> Similarly, a company sponsored reporter's "guide" for the media<sup>11</sup> and widely distributed press releases destined for public consumption<sup>12</sup> present hypoactive sexual desire disorder as an accepted and uncontroversial condition.

Asked about the widespread disagreement within the scientific community over how to define the condition, Proctor and Gamble's senior director of new drug development, Joan Meyer, agreed that defining female sexual problems was complex. But she defended company efforts to raise awareness about hypoactive sexual desire disorder, emphasising it was listed in established disease manuals. "We didn't make it up," she said.

## Controversy about the drugs

One of the biggest hurdles for drug makers in this area is showing a big enough benefit over placebo to outweigh concerns about short or long term side effects. These concerns are made more acute by recent revelations about hormone replacement therapy, antidepressants, and anti-arthritis drugs. At the December meeting, the FDA highlighted concerns about the potential long term risks of cardiovascular disease and breast cancer for those using the testosterone patch.<sup>13</sup> FDA reviewing medical officer Lisa Soule said that use of the patch was associated with higher than normal testosterone activity for an important minority of women in the company trials. She pointed out small, potentially troubling changes in several laboratory measurements and other indices, including blood

pressure, among women using the patch and oestrogen. The changes suggested that the drug combination may increase the risk of cardiovascular disease. Soule concluded that the short term nature of the 24 week placebo controlled randomised trials meant the regulator was "Unable to answer many questions about the safety of testosterone."

Expert adviser Steve Nissen, from the Cleveland Clinic, told the same meeting that in his view, based on the available data from the company's trials: "There was a high probability of excess cardiac risk with this product." Another panel member, Joanne Dorgan, noted that the heightened testosterone levels in some women using the patch could increase the risk of breast cancer. The trial data also showed small increases over placebo in minor side effects including acne, hair growth, and weight gain.<sup>14</sup>

Yet, in contrast, abstracts of data from the company's trials, presented by leading sex researchers at key international conferences, have simply concluded the testosterone patch is "well-tolerated." They have not mentioned potentially serious harms and have played down the small increases in milder side effects. The most recent abstract, presented in October 2004, states: "Overall, adverse event reports were similar in the testosterone and placebo groups."<sup>15</sup> Similarly, the slides from the company sponsored medical education package refer to the benefits of the patch but not its side effects. Sidney Wolfe, from the US consumer watchdog Public Citizen, told me that Proctor and Gamble is "Presenting a distorted view of its product by trivialising its risks."

While the possibly important risks of testosterone have been trivialised, the potentially modest benefits have been overblown. None of the key trials have been published in peer reviewed journals, but abstracts describing the company's data have been presented at several medical conferences in the United States and elsewhere in the past two years. The same data from the pivotal phase III trials have been presented at least twice, and data from one of the smaller phase II trials have been presented at least three times. Enthusiastic media coverage has often followed these presentations, most notably when a press release carried a headline suggesting the patch caused a "74 per cent increase in frequency of satisfying sexual activity."<sup>12</sup> This figure misleadingly describes the benefits in relative terms and gives no sense of the absolute benefits.

In absolute terms the trials showed the testosterone patch increased the amount of satisfying activity for women by around two "episodes" a month compared with baseline—but only one extra episode compared with the placebo response (table). Moreover, this extra

Preliminary results of 24 week randomised controlled trials of testosterone patch 300 µg/day in surgically menopausal women<sup>13</sup>

Outcome	Trial A (n=562)			Trial B (n=532)		
	Placebo	Patch	Difference	Placebo	Patch	Difference
Sexual activity (episodes/month)*	0.98	2.13	1.15	0.73	1.56	0.83
Sexual desire (100 point scale)†	6.9	11.85	4.95	6.21	11.38	5.17
Personal distress (100 point scale)	-16.31	-23.55	7.24	-18.27	-24.34	6.07

\*Increase from baseline of about 3 satisfying episodes a month.

†Change from baseline score of 20-23.

episode was on top of a baseline of around three sexual events a month, causing some researchers to question whether the women enrolled in the trials were really dysfunctional. "Three events per month, that's not a little," University of Amsterdam associate professor Ellen Laan told me, "That's quite average in the sort of long term relationships the women enrolled in these trials were having."

Harvard University associate professor Jan Shifren, a strong advocate of the testosterone patch, rejects the focus on the modest increases in sexual activity. She told me the key issue is how women feel about their desire problems. "The most important finding is the decrease in distress." Testosterone caused a significant decrease in distress compared with placebo, as measured by a company funded scale. Yet as FDA reviewers pointed out, the decrease over placebo was only 6 or 7 points on a 100 point scale. On a separate measure, testosterone increased a woman's level of desire over placebo by only 5 or 6 points on a 100 point scale, raising serious questions about the meaningfulness of these purported benefits (table).<sup>14</sup>

Although the FDA advisers ultimately voted to accept the patch benefits as "clinically meaningful," they unanimously rejected the company's data as inadequate to assess long term safety, and unanimously recommended the agency not to approve the drug. Proctor and Gamble's Plummer says the company is working with the regulator on the patch and looking to its leadership.

### Controversy about the conflicts of interest

As is now customary with new drug development, many of the experts involved in testing the patch, in advocating its approval, and in corporate attempts to "educate" doctors and the public, have a financial conflict of interest. At least two of the senior academic investigators also run private for-profit research companies that contract with Proctor and Gamble to help carry out the clinical trials. With such strong financial ties, the extent to which the role of these investigators is commercial or scientific comes into question. For example, one of those investigators, Wolf Utian from Rapid Medical Research, was unable to answer a basic question from me about the absolute size of the benefit the patch offered over placebo. He said he would have to go back and look at the data, because he didn't normally think about benefits in that way.

Another trial investigator, Harvard's Jan Shifren, initially tried to distance herself from Proctor and Gamble by saying she held no shares in the company. Yet after further questioning, Shifren disclosed she had presented at medical events funded by unrestricted educational grants from the company and that she was a paid member of the company's advisory board.

Psychologist Leonore Tiefer has closely tracked the marketing of female sexual dysfunction by Proctor and Gamble and other companies. She believes complex problems are too often being narrowly portrayed as due to a medical condition, "in order to build a market for drugs." As an alternative approach, her New View campaign<sup>16</sup> has helped spark a renewed debate about how to define women's sexual problems and generated a growing public scepticism, reflected in media investigations of the corporate sponsored creation of disease.<sup>17</sup>

### Summary points

Pharmaceutical companies have invested heavily in promoting a new condition called female sexual dysfunction

The scientific community disagrees about the scale and definition of the condition

Reports of drugs in development have underplayed the risks and overemphasised the benefits

Decisions about the condition and its treatment need to be based on unbiased research

The pharmaceutical industry's strong commercial interest in this area may ultimately bring benefits to women, through the development of safe and effective medicines, and through an increased understanding of female sexuality.<sup>10</sup> Yet if those desirable benefits are to be genuinely achieved, we might all have to start relying a little less on marketing and promotional campaigns about new diseases, dressed up as science and education.

Contributors and sources: RM is a journalist and has been reporting on medicine and health care for several years. This article is based on personal interviews and published resources.

Competing interests: RM is coauthor of *Selling Sickness*, which will be published later this year.

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